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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/073,334	02/13/2002	Steven J. Soldin	64688/155	6011

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EXAMINER	
GUPTA, ANISH	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 11/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/073,334	SOLDIN, STEVEN J.	
	Examiner	Art Unit	
	Anish Gupta	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 4-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 4-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The amendment filed 6-05-02 is acknowledged. Claim 1 was amended, claims 2-3 were canceled and page 29 was substituted. Claims 1, 4-8 are pending.

Specification

2. The abstract of the disclosure is objected to because the trademarks SANDIMMUNE and CYCLOTRAC, on page 11, do not have a proper notation to identify them as trademarks. The specification recites SANDIMMUNE ^{R} and CYCLOTRAC ^{R}. However, the appropriate format for trademarks is with a SANDIMMUNE ® and CYCLOTRAC®. Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 1, 4-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 state that the immunophilin exhibits a "Kd of about .8nm." It is unclear what activity is defined by "Kd." Applicants are requested to amend the claim to provide a more descriptive manner for the activity claimed.

In claim 7, the claim states that the immunophilin is recombinant with a molecular weight of 8.4 kDa and "with the properties exhibited by the immunophilin according to claim 1." However, claim 1 states that the immunophilin is isolated from soluble cytoplasm of lymphoid tissue. It is

unclear how a recombinant produced product can be isolated from soluble cytoplasm of lymphoid tissue. The claim is therefore indefinite.

Claim 8 recites the limitation "*said* isolated 8.4 kDa immunophilin". However, prior to this recitation, a reference to an 8.4 kDa immunophilin is not made and for this reason, there is insufficient antecedent basis for this limitation in the claim.

In claim 1 and 8, the claim recites "FK-506, rapamycin, or pharmacologically active metabolites or derivatives thereof." However, it is unclear what modification to the FK-506 or rapamycin are permissible to render FK-506 or rapamycin pharmacologically active metabobolite or derivative thereof. One of ordinary skill in the art does not know the meets and bounds of the claim and thus the claim is indefinite.

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4-8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that

> "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP 2163.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In Regents of the University of California v. Eli Lilly & Co., the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials. Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606; In re Smythe, 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus. . . ."). Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of

obtaining the claimed sequence." MPEP 2163. The MPEP does state that for generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative, the Courts have indicated what do not constitute a representative number species to adequately describe a broad generic. In Gostelli, the Court determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. In re Gostelli, 872 F.2d at 1012, 10 USPQ2d at 1618.

In the instant case, the claims are drawn to a derivatives of the FK-506 and rapamycin in claim 1 and 8. This generic statement for the derivative fails to adequately describe a structural feature common to the genus since the only common feature would be an amide bond between the amino acids for a derivatives is inclusive of any modification of the native FK-506 and rapamycin. The specification does not provide a single example of what qualify as derivatives of the claimed peptides. The specification, as a whole, does not sufficiently provide ample definition, such as by structure, formula, or chemical name, of the claimed subject matter sufficient to distinguish it from the native FK-506, rapamycin, and non-derivatives thereof. Accordingly, the disclosure lacks sufficient written description to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

As stated earlier, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable claims are broad generic with respect to derivatives. The possible structural variations are limitless, especially in the light of a lack of teachings for derivatives in the specification, since any side chain maybe modified, any amino acid may be deleted and/or any amino acid maybe substituted. Thus, so long as a peptide

has some biological activity, relative to the native, for any biological process, the peptide qualifies as a derivative. It must not be forgotten that the MPEP states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. Here the claims lack written description because there is no disclosure of a correlation between function and structure of the sequence. Moreover, the specification lack sufficient variety of species to reflect this variance in the genus since the specification does not provide any examples of derivatives. The specification is void of any peptides that contain structurally distinct substitutions that could be used as a benchmark for the definition of derivatives. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

1. Claims 1, 4-8 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 6,410,340. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons.

The claims are drawn to a immunophilin wherein it comprises a protein that has a molecular weight of 8.4 kDa, is isolated from the soluble cytoplasm of lymphoid tissue and has an N-terminal first 23 amino acid sequence according to Seq. Id. No. 1.

The US Patent claims a protein binding assay method for the imunosuppressant drugs FK-506, rapamycin, and pharmacologically active metabolites or derivatives thereof ("analytes"), in a fluid sample, comprising the steps of (a) contacting said fluid sample with an isolated about 8.4 kDa binding protein ("immunophilin") so that a complex forms between said analyte and said binding protein. The US patent states that the imunophilin exhibits the following characteristics: (i) wherein said isolated about 8.4 kDa immunophilin exhibits the following characteristics: (i) the first 23 amino acid sequence is identical to that of authentic ubiquitin; (ii) retention times on HPLC are identical to those of authentic ubiquitin; (iii) migrates on SDS-PAGE plates identically to HPLC-purified commercial ubiquitin; (iv) exhibits a Kd of about 0.8 nM for FK-506 and 0.08 nM for rapamycin; (v) has a Hill plot value of about unity; and (vi) when complexed to FK-506 inhibits calcineurin phosphatase activity (see claim 1 of the US patent). Note that the immunophilin claimed in the instant application has the same characteristics in molecular weight, the amino acid sequence,

and the same "kd" value (claimed in claim 4 of the instant application), the same hill plot value (claim 5), the same phophatase activity (claim 6).

Further, the kit claimed in claim 9 of the US patent is substantially identical to the Kit claimed in claim 8 of the instant application. Note the overlap between the components of the kit in the presence of the immunophilin and the labeled and unlabeled containers containing immunosuppressant drugs. Since the US Patent discloses an assay method which utilizes the same product that has been "isolated." This is especially true in light of claim 9 of the US patent which discloses the isolated immunophilin in a container. The difference between the US Patent and the instant application is that the US Patent does not teach the source of the product.

However, since the immunophilin product, between the US Patent claims and the instant application have the same molecular weight, the same N-terminal sequence and posses the same activity, the source would necessarily have to be the same. The MPEP states 'where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). 'When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.' In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. In re Best, *supra*. See also Titanium Metals Corp. v. Banner, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985)."

It is noted that the claims of the US patent are drawn to an assay method and the claims of the instant application are drawn to a product. Even though the claimed subject matter falls into

different statutory classes, the claims still render obvious one another because the US patent claims the an "isolated" immunphlin is used. Thus, in order to practice the claimed invention of the US Patent one would necessarily have to have the product claimed in the instant application. Based on this, the claims (US patent and instant application) overlap significantly to render them as not patentably distinct from each other.

2. The claims of the instant application are free of prior art. The closest art, Wang et al., teaches a peptide with the N-terminal sequence as claimed in the instant claims (see page 482 defined as PK21). However, the molecular weight disclosed by the reference does not meet the molecular weight claimed. Note the reference teach the molecular weight as 8.589 kDa. This is outside the claimed molecular weight of 8.4 kDa. Further, the reference does not teach the source or activity as claimed in claim 1.

3. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anish Gupta whose telephone number is (703) 308-4001. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback , can normally be reached on (703)306-3220. The fax phone number of this group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

11/17/05

Anish Gupta
Patent Examiner